acquired infections. Antibiotics were not given before blood culture (BC) collection in only 3 of 9 patients (*C.burnetii* 1, *S.oralis* 2). Mean time of antibiotics given before valve surgery was 29 ± 15 days. Predisposing conditions were interventricular septum 1, rheumatic valvulopathy 4, prosthesis 3. All transesophageal echocardiograms showed major criteria, but all cases were only clinically possible by the modified Duke criteria. All cases were definite by surgical and histopathological and immunohistochemistry findings. Clinical features showed fever in 4/9, new valvar regurgitation in all, splenomegaly in 1/9, emboli to skin in 1/9, elevated CRP in 6/6, and elevated ESR in 5/7 patients. Two patients died, both in refractory heart failure.

Conclusion: The gold standard to establish the etiology of BCNE is study of the excised valves. Nearly a third of cases of BCNE in this cardiac surgery hospital had its etiology defined by PCR of paraffin-embedded valves. This is the first data from Brazil relying on molecular biology of valves for the diagnosis of BCNE, with viridans, *Coxiella* and *Bartonella* documented. Of note, 7 of the 9 cases involved *S.oralis* underscoring antibiotics prior to BC collection as a major factor in BC negativity.

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Successful short antibiotic treatment of childhood pneumonia - Myth or reality? (Invited Presentation)

22.001

Determinants of Bacteriologic Eradication in Respiratory Tract Infections

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Understanding of the relationships between pharmacokinetic (PK) and pharmacodynamic (PD) parameters and bacteriological and clinical outcomes of infections has resulted in appreciation of the correlation between in vitro potency and in vivo efficacy of antimicrobial agents. PK and PD principles can be applied to the development of new antibacterials and optimising the formulation of existing agents to help address the increasing prevalence of antibacterial resistance. Antimicrobial agents can generally be divided into those that have time-dependent activity, such as beta-lactams, and those that have concentration-dependent activity, such as macrolides, lincosamides and quinolones. For beta-lactams, the unbound serum concentration of the drug exceeding the minimum inhibitory concentration of the causative pathogen for 40-50% of the dosing interval (40% for penicillins and 50% for cephalosporins) is predictive of bacteriologic efficacy and can be used to determine a PK/PD breakpoint for specific dosing regimens. For concentration-dependent agents, the unbound serum area-under-the-curve (AUC) to MIC ratio exceeding 30 for macrolides, lincosamides and quinolones is generally predictive of bacteriologic efficacy and can be used to determine a PK/PD breakpoint for these agents. Amoxicillin and amoxicillin/clavulanate are examples of agents that have been studied and PK/PD principles applied agement of respiratory tract infections despite development of resistance. While intrinsic and acquired resistance is common in respiratory pathogens, in vitro susceptibility can be accurately interpreted based on PK/PD parameters. PK/PD principles can be used to develop effective dosing regimens, develop new formulations and dosage regimens, contribute to guideline recommendations, establish susceptibility breakpoints, and validate bacteriologic outcome in clinical studies. However, PK/PD principles do not relate to length of therapy, which is mainly influenced by disease severity, presence of comorbid conditions and patient compliance.

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22.002

What Are the Benefits of Short Antibiotic Treatment?

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Most antibiotics prescribed for outpatients are written for treatment of respiratory tract infections. Many of these prescriptions are necessary for curbing spread of infection and preventing development of harmful sequelae. Less attention has been paid to the role of duration of antibiotic therapy to treat respiratory tract infections, particularly pneumonia in children, for the judicious use of antibiotics. In fact, prescribing the appropriate duration of a course of antibiotic therapy is as important as eliminating prescriptions for nonbacterial illnesses in practising judicious use of antibiotics.

How long is enough and how long is too much? Therapeutic courses need to be of sufficient duration to result in a clinical cure to return patients as rapidly as possible to normal functioning and to prevent the progression of disease and the development of dangerous sequelae. However, unnecessarily lengthy courses of therapy may prevent the realization of these treatment goals by heightening the risk of development of bacterial resistance and side effects and by reducing compliance with the therapeutic regimen. In children, the latter is however not relevant. We investigated the direct impact of antibiotic exposure on resistance at the individual level in healthy cohorts, treated with azithromycin, clarithromycin, or a placebo in a randomised, double-blind trial. Both macrolides significantly increased the mean macrolide-resistant proportions of viridans streptococci compared to the placebo at all time-points. Our study showed that selection of resistance occurs very rapidly after the exposure to antibiotics, peaking in the immediate post-therapy period. In conclusion, decrease of side-effects could be the main benefit of shorter antibiotic treatment.

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